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PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Burton G. CHRISTENSEN et al.	)	Group Art Unit: 1639
	)	
Application No.: 09/457,926	)	Examiner: Mark Shibuya
	)	
Filed: December 8, 1999	)	
	)	
For: NOVEL ANTIBACTERIAL AGENTS	)	Confirmation No.: 8221

Attention: Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY BRIEF UNDER 37 C.F.R. § 41.41

Pursuant to 37 C.F.R. § 41.41, Appellants present this Reply Brief in response to the Examiner's Answer dated April 18, 2007. Appellants previously filed a Request for Oral Hearing on January 12, 2007.

If there are any fees due in connection with the filing of this Reply Brief that are not enclosed herewith, please charge such fees to our Deposit Account No. 06-0916.

I. INTRODUCTION

Appellants submit this Reply Brief to address several erroneous assertions set forth in the Examiner's Answer.[1] More specifically, despite maintaining the rejection of claims 41, 43, 49-51, and 53-55 under 35 U.S.C. § 103(a) over Truett I (U.S. Patent No. 5,963,791) in view of

[1] Appellants have endeavored to address assertions in the Examiner's Answer without unduly repeating the same arguments in Appellants' Opening Brief.

Truett II (U.S. Patent No. 6,437,119), Boeckh, Renoud-Grappin, and Staroske, the Office has continued to ignore that fact that the Office's proposed modification would destroy the intended function of the cited references.

Several basic factual inquires must be made in order to determine the obviousness or non-obviousness of claims of a patent application under 35 U.S.C. § 103, and these factual inquiries, set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), require the Office to:

(1) Determine the scope and content of the prior art;

(2) Ascertain the differences between the prior art and the claims in issue;

(3) Resolve the level of ordinary skill in the pertinent art; and

(4) Evaluate evidence of secondary considerations.

The obviousness or non-obviousness of the claimed invention is then evaluated in view of the results of these inquiries. *Graham*, 383 U.S. at 17-18, 148 USPQ 467; *see also KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1730 (2007).

Thus, in order to satisfy the initial burden of establishing a prima facie case of obviousness, the Office must consider the references as a whole, and show that there is some reasoning, either in the references or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the references in the manner proposed by the Office. *In re Rouffet*, 149 F.3d 1350, 47 USPQ.2d 1453 (Fed. Cir. 1998). The Supreme Court mandates that "[t]o facilitate review, this analysis [of whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue] should be made explicit." *KSR*, 127 S. Ct. at 1741. (citing *In re Kahn*, 441 F.3d 977, 988 (Federal Circuit, 2006) ("[R]ejections

on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness")). In the present case, however, the Office once again bases its obviousness rejection on the general goal or desire to obtain a broad spectrum antibiotic while ignoring the scope of the cited references. *See Graham*, 383 U.S. at 17-18. For the reasons presented here and in Appellants' Opening Brief, the Office's 35 U.S.C. § 103 rejection is improper and should be reversed

II. ARGUMENT IN REPLY

A. The Office Cannot Modify the Art in a Manner That Would Destroy the Intended Function of the Disclosed Compounds

In its Opening Brief, Appellants argued that Truett II discloses a three-antibiotic compound consisting of ceftazidime, a quinolone, and vancomycin, and that by eliminating the quinolone to obtain the presently claimed invention, as suggested by the Office, the intended function of the three-antibiotic compound disclosed in Truett II would be destroyed. *See* Opening Brief at 11-13. In response, the Office states:

> appellant has not provided evidence or reasons as to why an obvious dimeric antibiotic composition of a beta lactam and a vancomycin would represent a modification to the trimeric antibiotic composition of Truett II such that the antibiotic composition would not work for its intended purpose.

Examiner's Answer at 16. The Office's contention, however, has no basis in fact once Truett II is considered as a whole, as required by *Graham*.

To begin with, Appellants have provided ample evidence that modification of Truett II's "trimeric" antibiotic composition, by eliminating the quinolone to form the dimeric antibiotic composition of the presently claimed invention, would destroy the intended function of the

disclosed compounds. For instance, Truett II explicitly states throughout that the "value" of the disclosed compositions resides in the "trio" of antibiotics. *See* Truett II at col. 1, lines 22-31. The only example in Truett II is directed to the three-component antibiotic. *Id.* at col. 24, line 50 to col. 25, line 43. And Truett II specifically directs one of skill in the art to add a third antibiotic, such as vancomycin, to the "bi-component" composition. *Id.* at col. 1, lines 16-21. Even the Office acknowledges that the "value" in Truett II's compositions is derived from the three-antibiotic combination. *See* Examiner's Answer at 16. These statements establish that the success of Truett II's compositions is due to its three-component structure.

The Office has not provided any evidence, other than an unsupported generalized statement, that removal of a component of Truett II's three-antibiotic compound would result in a functioning two-antibiotic compound. There is simply nothing in Truett II, or any of the other cited references, establishing that the combination of ceftazidime and vancomycin would lead to the results disclosed in Truett II. *In re Fritch*, 972 F.2d 1260, 1265 n.12, 23 U.S.P.Q.2d 1780, 1783 n. 12 (Fed. Cir. 1992) ("A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose."); *In re Ratti*, 270 F.2d 810, 813, 123 U.S.P.Q. 349, 352 (C.C.P.A. 1959) (holding the suggested combination of references improper under § 103 because it "would require a substantial reconstruction and redesign of the elements shown in [a prior art reference] as well as a change in the basic principles under which [that reference's] construction was designed to operate").

In an attempt to rebut this conclusive evidence, the Office contends that:

> the value of the disclosed composition is that the bacterial infective agent will be simultaneously attacked by the linked trio of agents which are known to attack the cell-wall producing enzyme of the bacteria, and that emergence of resistance against the antibiotics will be prevented.
>
> These same "values", which the examiner respectfully submits are tantamount to uses or functions, are also attributed to composition that are made by linking two antibiotic moieties, as taught by the prior art.

Examiner's Answer at 16-17. But the Office's response is nothing more than a generalized goal for any antibiotic compound—attacking the bacteria and prevent antibiotic resistance. Truett II achieved this generalized goal by using a three-antibiotic composition. And moreover, although Truett I discloses a two-antibiotic compound, it does not disclose a compound where ceftazidime is linked to vancomycin. In fact, one should consider the fact that Truett I's later work, reflected in Truett II, indicates that if ceftazidime is linked to vancomycin, this should be done ***only*** in a three-antibiotic compound.

Based on a review of the prior art as a whole, it is entirely improper for the Office to make generalized and unsupported statements that a two-antibiotic compound would possesses the same "value" as the three-antibiotic compound disclosed in Truett II. Again, as recently emphasized by the Supreme Court in KSR, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR*, 127 S. Ct. at 1741.

Finally, the Office asserts that "one of skill in the art would not find that the dimeric compound of the *primary* reference of Truett I, would be rendered inoperable by the modification of substituting a vancomycin compound into the dimeric compound." Examiner's

Answer at 19 (emphasis in original). The problem, however, is that the Office provides no support for this contention and ignores the scope of the prior art.

Truett I does disclose two-antibiotic compositions, but none containing vancomycin. Boeckh discloses the use of ceftazidime in a mixture with vancomycin, but not as a linked compound (Boeckh at 92), and Truett II, the same inventor as Truett I, discloses the combination of ceftazidime and quinolone with the option of adding vancomycin to this two-antibiotic composition. To follow the Office's logic to achieve the claimed invention would destroy the intended function of the compounds disclosed in the prior art. Such a result cannot support an obviousness rejection.

B. Truett II Does Teach Away From the Claimed Invention

Contrary to the Office's position (Examiner's Answer at 19-20), Truett II does teach away from making a two-component antibiotic consisting of ceftazidime and vancomycin. This is particularly true when one considers the fact that Truett II and Truett I are from the same inventor—that is, when the scope of the prior art is considered as a whole.

The only two-component antibiotic disclosed in Truett II consists of linking a quinolone antibiotic to a beta-lactam antibiotic such as ceftazidime. Truett I also discloses a two-antibiotic compound but none with ceftazidime and vancomycin. Thus, considering the scope of the prior art, the references disclose two-antibiotic compounds that do not contain vancomycin. And in view of Truett II, if vancomycin is used, it is only as part of a three-component antibiotic with quinolone and ceftazidime present. The scope of Truett I and Truett II specifically teach away from a two-antibiotic composition consisting of ceftazidime and vancomycin.

The Office further contends that "the linked antibiotics of Truett II are structurally similar to the instant compound." *Id.* at 20. The Office is not correct. The Office must compare the differences between the claimed invention and the prior art. *See Graham*, 383 U.S. at 17-18. When one compares the claimed invention (two antibodies joined together by a linker group), to Truett II (a three-antibody compound), it is clear that the compounds of Truett II are not structurally similar to the instant claims. Appellants contend that a compound consisting of three antibiotics is not structurally similar to a composition consisting of two antibiotics.

C. The Office's Obviousness Rejection Is Based on Hindsight Reasoning

The Office has not adequately addressed Appellants' contention that the selection of ceftazidime out of the 69 compounds disclosed in Truett I was based on hindsight reasoning. The Office asserts that the selection of ceftazidime is not "an unreasonable or arbitrary choice . . ." given the "guidance provided by Truett I, in its disclosed classification of antibiotics based upon a ***common molecular structure***." Examiner's Answer at 22-23 (emphasis added). But the Office has not explained how Truett I's alleged guidance to select an antibiotic based on "common molecular structure" directs one skilled in the art to select ceftazidime. In fact, the Office's statement that "there were a multitude of microbial agents at the time of the claimed invention" only supports Appellants' argument that the Office selected ceftazidime from the "multitude of microbial agents" only after considering Appellants' invention.

Taking into consideration only the cephalosporins disclosed in Truett I, this class of antibiotics still consists of 17 compounds, all with a common core molecular structure. Truett I at col. 2, line 59 - col. 3, line 14. Based on the Office's logic, Truett I, at most, would provide guidance to select these 17 compounds. But Truett I must be considered as a whole.

See Graham, at 17-18. When considered as a whole, Truett I discloses nine classes of antibiotic compounds wherein the compounds of each class share a common molecular structure. And within these nine classes, Truett I discloses 69 individual compounds. Even if one were to assume for arguments sake that "common molecular structure" provides guidance, Truett I still fails to provide the requisite guidance to select cephalosporins from the nine classes (and 69 compounds) disclosed, and then further select ceftazidime from the 17 other cephalosporins disclosed in the reference. It is only with Appellants' application in hand that the Office was able to select ceftazidime. As such, it is clear that the Office's § 103 rejection is impermissibly based on hindsight reasoning.

D. Boeckh, Renoud-Grappin, and Staroske Do Not Bolster the Office's Obviousness Rejection

The Office contends that one of skilled in the art would be motivated to combine ceftazidime and vancomycin because Boeckh discloses that "vancomycin is used in combination with ceftazidime as a broad spectrum treatment for gram positive and gram negative bacterial infections[,]" Truett I discloses that two antibiotic moieties (one that attacks gram positive and one that attacks gram negative bacteria) can be linked, and Truett II discloses the linkage of "ceftazidime, with vancomycin as part of a heterotrimeric compound, which also includes quinolone." Examiner's Answer at 23-24. The Office's argument fails because Boeckh teaches that the combination of ceftazidime and vancomycin, as a mixture as opposed to a linked composition, shows "excellent clinical response . . . ." Boeckh at 94, right column. Given the lack of any disadvantage of using a mixture of ceftazidime and vancomycin, one of skill in the

art would not be motivated to link the two compounds. *See Winner Int'l Royalty Cor v. Wang*, 202 F.3d 1340, 1349, 53 U.S.P.Q.2d 1580, 1587 (Fed. Cir. 2000).

In an attempt to circumvent Appellants' argument, the Office contends that Boeckh "does not stand for the proposition that the combination cocktail of ceftazidime and vancomycin is perfected to the degree such that one of ordinary skill would not be motivated to modify the composition of Boeckh." Examiner's Answer at 26. To support this contention, the Office quotes from the first paragraph of the reference. *Id.* The first paragraph of Boeckh, however, simply sets forth the basis for studying the "pharmacokinetics and serum bacterial activity of vancomycin-ceftazidime." Boeckh at 92, left column. This paragraph does not indicate that the effectiveness of a vancomycin and ceftazidime mixture has not been adequately studied, as offered by the Office, but rather that ***because of*** the known effectiveness of the combination of the two compounds in a mixture, the pharmacokinetics of such a combination need to be evaluated. *Id.* Given the positive results obtained in Boeckh, one skilled in the art would continue to use vancomycin and ceftazidime in a mixture as opposed to a linked two-component antibiotic.

With respect to Renoud-Grappin, Appellants do not contest that the reference suggests linking compounds, but those compounds are anti-virals, not antibiotics. Moreover, the Office has failed to point to any disclosure in Renoud-Grappin that linking two compounds, as opposed to mixing them together as in Boeckh, leads to an improved result. Thus, when considering the prior successful use of ceftazidime in a mixture with vancomycin as disclosed in Boeckh (in essence considering the scope of the prior art as the Office must do), Renoud-Grappin provides no motivation to link the two compounds.

Finally, the Office again asserts that Staroske suggests the use of "homodimers" of linked vancomycin to create more potent antibiotics. *See* Examiner's Answer at 25. But Staroske's disclosure of a vancomycin-vancomycin antibiotic does not lead to the creation of a two-antibiotic composition consisting of ceftazidime joined to vancomycin by a linker.

Conclusion

For the reasons set forth above and in Appellants' Opening Brief, the Office's rejections under 35 U.S.C. §103 are improper and should be reversed.

Respectfully submitted,

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